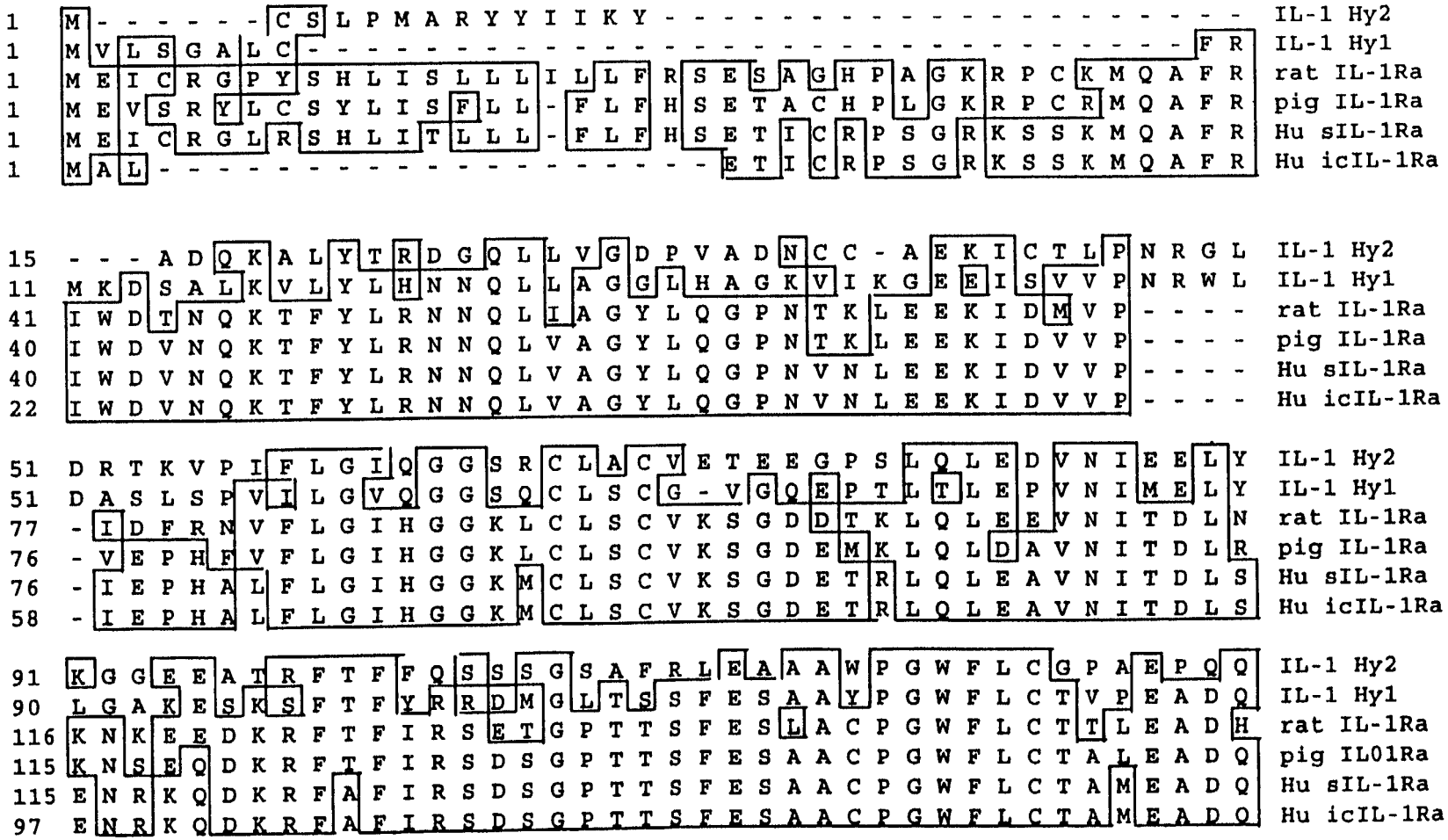


Fig.1A

```
131 P V Q L T K E S E P S A R - - - - T K F Y F E Q S W   IL-1 Hy2
130 P V R L T Q L P E N G G W N A P I T D F Y F Q Q C D   IL-1 Hy1
156 P V S L T N T P K E P - - - C T V T K F Y F Q E D Q   rat IL-1Ra
155 P V G L T N T P K A A - - - V K V T K F Y F Q Q D Q   pig IL-1Ra
137 P V S L T N M P D E G - - - V M V T K F Y F Q E D E   Hu sIL-1Ra
137 P V S L T N M P D E G - - - V M V T K F Y F Q E D E   Hu icIL-1Ra
```

Decoration 'id-consensus': Box residues that match the Consensus exactly.

Fig.1B

FIGURE 2A

SEQ ID NO.: 12

```
        10         20         30         40         50         60
GGCAGTGGGA CTGGGTTTGA GCTGGGCTTA TCCTCCAACT GTGAGGGAGG CTACAGCACA 60
CTCCACCCCA CTCTCAGGGC TGGGAATTGT TGTGGCTCAG CTATTTGGGG GAATCTGTTT 120
TCCAGTTTCT CAGAACCAGC GCAAGCACAC ACATCCCAGG CTCACACCCC TGGTGGCTGG 180
ACTTGCTCCC GGATAGCCTC AGTCAGGGAG AGGCAGAGCT GCCTGGAGCC TGCTGGGCTG 240
GTGGAAGCCT TGGTGGATTC TGGCAGGCCA ATTATAGATG AATGGCCTGG GGAACCCGTG 300

       310        320        330        340        350        360
CAGCCCGTGG CTGAGTGGTT CTAAGCCCCA GCACGTCTGC CTCTGGCTTC ACCCAGCCTC 360
CTTTTCTAAC TGCCCTTCTC TCCTCCCCAT CAGTGAGGAC CAGACACCAC TGATTGCAGG 420
AATGTGTTCC CTCCCCATGG CAAGATACTA CATAATTAAA TATGCAGACC AGAAGGCTCT 480
ATACACAAGA GACGGCCAGC TGCTGGTGGG AGATCCTGTT GCAGACAACT GCTGTGCAGA 540
GAAGATCTGC ACACTTCCTA ACAGAGGCTT GGACCGCACC AAGGTCCCCA TTTTCCTGGG 600

       610        620        630        640        650        660
GATCCAGGGA GGGAGCCGCT GCCTGGCATG TGTGGAGACA GAAGAGGGGC CTTCCCTACA 660
GCTGGAGGAT GTGAACATTG AGGAACTGTA CAAAGGTGGT GAAGAGGCCA CACGCTTCAC 720
CTTCTTCCAG AGCAGCTCAG GCTCCGCCTT CAGGCTTGAG GCTGCTGCCT GGCCTGGCTG 780
GTTCCTGTGT GGCCCGGCAG AGCCCCAGCA GCCAGTACAG CTCACCAAGG AGAGTGAGCC 840
CTCAGCCCGT ACCAAGTTTT ACTTTGAACA GAGCTGGTAG GGAGACAGGA AACTGCGTTT 900
```

FIGURE 2B

```
       910        920        930        940        950        960
TAGCCTTGTG CCCCCAAACC AAGCTCATCC TGCTCAGGGT CTATGGTAGG CAGAATAATG 960
TCCCCCGAAA TATGTCCACA TCCTAATCCC AAGATCTGTG CATATGTTAC CATACATGTC 1020
CAAAGAGGTT TTGCAAATGT GATTATGTTA AGGATCTTGA AATGAGGAGA CAATCCTGGG 1080
TTATCCTTGT GGGCTCAGTT TAATCACAAG AAGGAGGCAG GAAGGGAGAG TCAGAGAGAG 1140
AATGGAAGAT ACCATGCTTC TAATTTTGAA GATGGAGTGA GGGGCCTTGA GCCAACATAT 1200

      1210       1220       1230       1240       1250       1260
GCTTGTGTTT TTAGAAGGAG GAAAAGCCAA GGGAACGGAT TCTCCTCTAT AGTCTCCGGA 1260
AGGAACACAG CTCTTGACAC ATGGATTTCA GCTCAGTGAC ACCCATTTCA GACTTCTGAC 1320
CTCCACAACT ATAAAATAAT AAACTTGTGT TATTGTAAAC CTCTGG 1366
```

FIGURE 3

SEQ ID NO.: 13

```
         10         20         30         40         50
MNGLGNPCSP WLSGSKPQHV CLWLHPASFS NCPSLLPISE DQTPLIAGMC  50
SLPMARYYII KYADQKALYT RDGQLLVGDP VADNCCAEKI CTLPNRGLDR 100
TKVPIFLGIQ GGSRCLACVE TEEGPSLQLE DVNIEELYKG GEEATRFTFF 150
QSSSGSAFRL EAAAWPGWFL CQPAEPQQPV QLTKESEPSA RTKFYFEQSW 200
```

FIGURE 4A

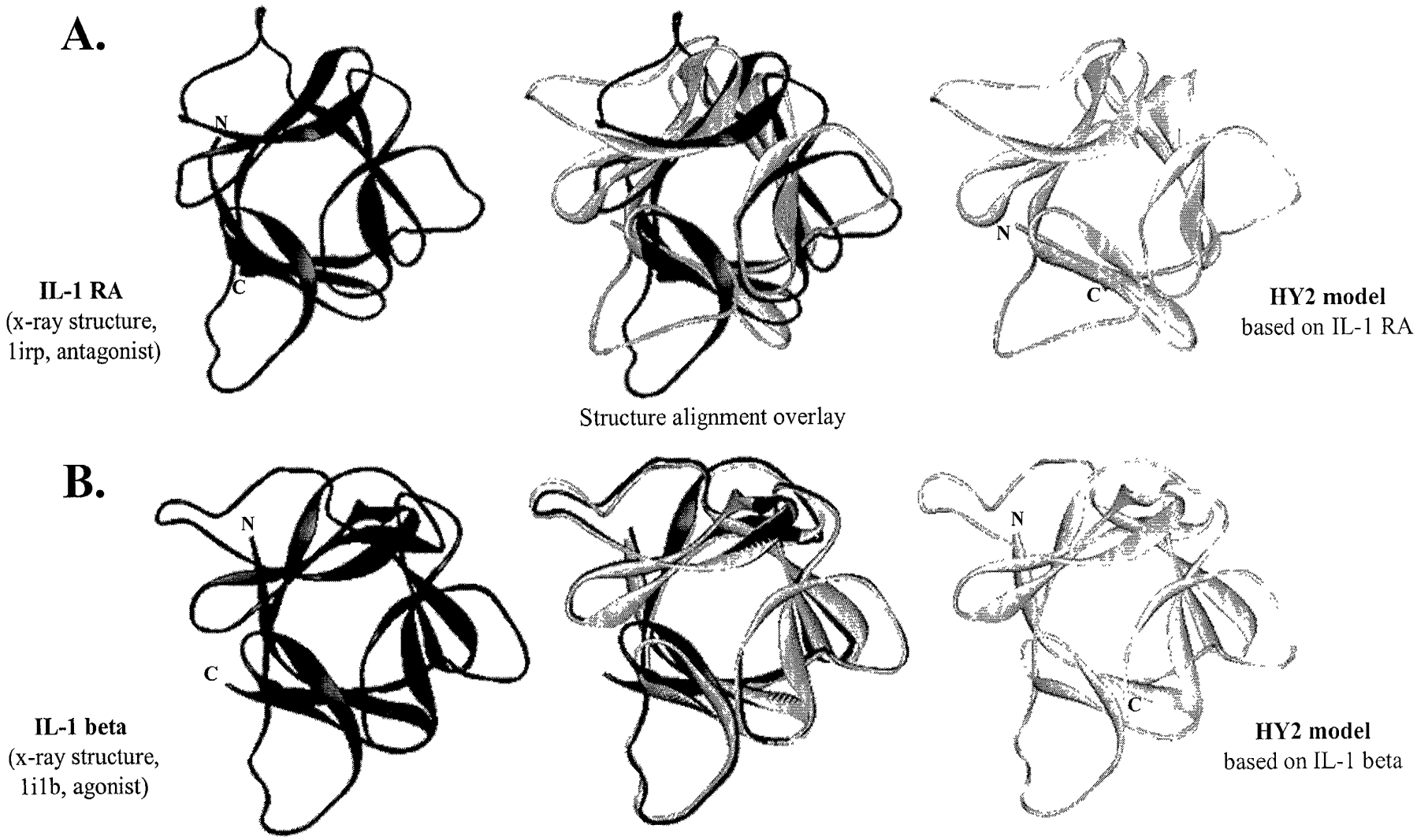
SEQ ID NO.: 14

```
        10         20         30         40         50         60
GGCAGTGGGA CTGGGTTTGA GCTGGGCTTA TCCTCCAACT GTGAGGGAGG CTACAGCACA     60
CTCCACCCCA CTCTCAGGGC TGGGAATTGT TGTGGCTCAG CTATTTGGGG GAATCTGTTT    120
TCCAGTTTCT CAGAACCAGC GCAAGCACAC ACATCCCAGG CTCACACCCC TGGTGGCTGG    180
ACTTGCTCCC GGATAGCCTC AGTCAGGGAG AGGCAGAGCT GCCTGGAGCC TGCTGGGCTG    240
GTGGAAGCCT TGGTGGATTC TGGCAGGCCA ATTATAGACG AATGGCCTGG GGAACCCGTG    300

       310        320        330        340        350        360
CAGCCCGTGG CTGAGTGGTT CTAAGCCCCA GCACGTCTGC CTCTGGCTTC ACCCAGCCTC    360
CTTTTCTAAC TGCCCTTCTC TCCTCCCCAT CAGTGAGGAC CAGACACCAC TGATTGCAGG    420
AATGTGTTCC CTCCCCATGG CAAGATACTA CATAATTAAA TATGCAGACC AGAAGGCTCT    480
ATACACAAGA GACGGCCAGC TGCTGGTGGG AGATCCTGTT GCAGACAACT GCTGTGCAGA    540
GAAGATCTGC ACACTTCCTA ACAGAGGCTT GGACCGCACC AAGGTCCCCA TTTTCCTGGG    600

       610        620        630        640        650        660
GATCCAGGGA GGGAGCCGCT GCCTGGCATG TGTGGAGACA GAAGAGGGGC CTTCCCTACA    660
GCTGGAGGAT GTGAACATTG AGGAACTGTA CAAAGGTGGT GAAGAGGCCA CACGCTTCAC    720
CTTCTTCCAG AGCAGCTCAG GCTCCGCCTT CAGGCTTGAG GCTGCTGCCT GGCCTGGCTG    780
GTTCCTGTGT GGCCCGGCAG AGCCCCAGCA GCCAGTACAG CTCACCAAGG AGAGTGAGCC    840
CTCAGCCCGT ACCAAGTTTT ACTTTGAACA GAGCTGGTAG GGAGACAGGA AACTGCGTTT    900
```

FIGURE 4B

```
        910         920         930         940         950         960
TAGCCTTGTG CCCCCAAACC AAGCTCATCC TGCTCAGGGT CTATGGTAGG CAGAATAATG    960
TCCCCCGAAA TATGTCCACA TCCTAATCCC AAGATCTGTG CATATGTTAC CATACATGTC   1020
CAAAGAGGTT TTGCAAATGT GATTATGTTA AGGATCTTGA AATGAGGAGA CAATCCTGGG   1080
TTATCCTTGT GGGCTCAGTT TAATCACAAG AAGGAGGCAG GAAGGGAGAG TCAGAGAGAG   1140
AATGGAAGAT ACCATGCTTC TAATTTTGAA GATGGAGTGA GGGGCCTTGA GCCAACATAT   1200

       1210        1220        1230        1240        1250        1260
GCTTGTGTTT TTAGAAGGAG GAAAAGCCAA GGGAACGGAT TCTCCTCTAT AGTCTCCGGA   1260
AGGAACACAG CTCTTGACAC ATGGATTTCA GCTCAGTGAC ACCCATTTCA GACTTCTGAC   1320
CTCCACAACT ATAAAATAAT AAACTTGTGT TATTGTAAAC CTCTGG 1366
```

Figure 5



Atty Docket No. 28110/36858A
Title: Novel Interleukin-1 Hy2 Materials and Methods
Inventors: Mize et al.
Figure 5
Sheet 8 of 10

Figure 6

Sequence Alignment based on 2° Structure

Hy2 and IL-1 RA (antagonist)

```
                ----1->      -2-->  ----3-->        --4-->            --5->
IL-1RA:  10  MQAFRIWDVNQKTFYLRNNQLVAGYLQGPNVNLEEKIDVVPIEPHA-----LFLGIHGGK 64
              + + I    +QK  Y R+ QL+ G      N     EKI ++P           +FLGI GG
Hy2    : 1   ARYYIIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLDRTKVPIFLGIQGGS 59

                ---6-->   ----7---> variable dom.  --8-->  --9->       -10->
IL-1RA:  65  MCLSCVKSGDETRLQLEAVNITDLSENRKQDKRFAFIRSDSGPTTSFESAACPGWFLCTA 124
              CL+CV++ +    LQLE VNI +L +  ++  RF F +S SG      E+AA PGWFLC
Hy2    : 60  RCLACVETEEGPSLQLEDVNIEELYKGGEEATRFTFFQSSSGSAFRLEAAAWPGWFLCGP 119

                   --11->           --12-->
IL-1RA:  125 MEADQPVSLTNMPDEGVMVTKFYFQEDE 152
              E  QPV LT     E     TKFYF++
Hy2    : 120 AEPQQPVQLTKES-EPSARTKFYFEQSW 146
```

SEQ ID NO: 21

SEQ ID NO: 22

SEQ ID NO: 21

SEQ ID NO: 22

SEQ ID NO: 21

SEQ ID NO: 22

--β-strand-->

SEQ ID NO:22 = amino acid 7-153 of SEQ ID NO: 2

Figure 7

Sequence Alignment based on 2° Structure

Hy2 and IL-1 beta (agonist)

```
                ---1---->   ---2--->  ----3--->    -----4---->    ----5---->
IL-1β: 3    VRSLNCTLRDSQQKSLVMSGPYELKALHLQGQDMEQQVVFSMSFVQGEESNDKIPVALGL 62
         +    ++ + QK+L      +L        +   +    +   +G +   K+P+ LG+
Hy2  : 1    PMARYYIIKYADQKALYTRDG-QLLVGDPVADNCCAEK-ICILPNRGLDRT-KVPIFLGI 57

                ----6----> -----7----->          ---8--->  --10-->    -11-
IL-1β: 63   KEKNLYLSCVLKDDKPTLQLESVDPKN-YPKKKMEKRFVFNKIEINNKLEFESAQFPNWY 121
         +  +  L+CV  ++ P+LQLE V+ +  Y   +   RF F +    +    E+A +P W+
Hy2  : 58   QGGSRCLACVETEEGPSLQLEDVNIEELYKGGEEATRFTFFQSSSGSAFRLEAAAWPGWF 117

                 -->     --12-->     -----13--->
IL-1β: 122  ISTSQAENMPVFLGGTKGGQDITDFTMQFVSS 153
         +         PV L         T F  +
Hy2  : 118  LCGPAEPQQPVQLTKESEPSARTKFYFEQSW  148
```

SEQ ID NO: 23

SEQ ID NO: 24

SEQ ID NO: 23

SEQ ID NO: 24

SEQ ID NO: 23

SEQ ID NO: 24

--β-strand-->

SEQ ID NO: 24 = amino acid 5-153 of SEQ ID NO: 2